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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
STEADMAN,D	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/529,043	Applicant(s) EIKMANNS ET AL.	
	Examiner David J. Steadman	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17 and 32-51* is/are pending in the application.

4a) Of the above claim(s) *1-17 and 32-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 1-17 and 32-51 are pending in the application.

Applicants election with traverse of Group II, claims 38-51, drawn to a pyruvate carboxylase (pyc) gene and a vector and host cells comprising said gene, cancellation of claims 18-31, and addition of claims 38-51 in Paper No. 10 is acknowledged.

Applicants traverse the lack of unity on the grounds that the instant application is entitled to the benefit of priority of a German application filed 4 October 1997 and therefore, because the examiner applied a reference with a publication date of April 1998, pyc genes or allelic variants thereof were not known in the art. This argument is not found persuasive. Applicants have claimed benefit of two German priority documents, namely German Application No. 19743894.6 with a filing date of 4 October 1997 and German Application No. 19831609.7 with a filing date of 14 July 1998. Applicants have provided no English-language translations of the German priority documents and the examiner has no knowledge of the German language. Therefore, the examiner has no method of determining which of the two German priority dates the claimed subject matter of the instant application should receive. Therefore, the examiner properly applied a reference with a publication date of April 1998 in making a lack of unity. In order to avoid further misunderstandings regarding the German priority dates, the examiner has elected to apply a different reference in making a lack of unity. The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical feature for the following reasons: a "substantially identically-effective DNA sequence" of a pyruvate carboxylase gene as

encompassed by claim 39 was known in the art at the time of the invention (see for example Morris et al. Biochem Biophys Res Commun 145:390-6).

Applicants further argue the claims of Groups I and III are directed to the same invention and therefore, no lack of unity should be applied to the claims of these Groups. This argument is not found persuasive. A search of each Group would require independent considerations which would require the examiner to focus on different features and entail differently structured word searches for both patent and non-patent literature for each of the three groups. For example, the claims of Group I are drawn to methods of amino acid production using an "enhanced export carrier" and microorganisms with a "higher proportion of the central metabolism metabolites" that are not recited in the claims of Group III. Thus co-examination of the inventions listed as Groups I and III would require a serious burden of search on the examiner.

Claims 1-17 and 32-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim.

The requirement is still deemed proper and is therefore made FINAL.

Applicants' request for interference between the instant application and US Patent 6,171,833 is acknowledged. Applicants' attention is directed to MPEP 2306 and 37 CFR 1.606 regarding interference between an application and a patent, which states, "The application must contain, or be amended to contain, at least one claim that is patentable over the prior art and corresponds to each count." At present, none of the elected claims are in condition for allowance. Upon allowance of claimed subject matter, an interference will be considered as per applicants' request.

Drawings

1. The drawings are objected to by the Draftsperson. See the attached "Notice of Draftsperson's Patent Drawing Review". Direct any inquiries concerning drawing review to the Drawing Review Branch (703) 305-8404.

Sequence Compliance

2. This application contains sequence disclosures (see for example, page 10 of the instant specification) that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825; applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). To be in compliance, applicants must provide an initial computer readable form (CRF) copy of the "Sequence Listing", an initial paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, and a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d). Applicant is requested to return a copy of the attached Notice to Comply with the response.

Specification/Informalities

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "Nucleic Acid Encoding Pyruvate Carboxylase From *Coryneform glutamicum*". See MPEP § 606.01.

4. The specification is objected to because there is no "Brief Description of the Drawings" section. See MPEP § 608.01(f).

Claim Objections

5. Claims 38-40 are objected to because the use of "SEQ ID No." is improper and should be replaced with "SEQ ID NO:". Appropriate correction is required.

6. The term "pyruvate-carboxylate" in claim 41 is misspelled and should be replaced with "pyruvate-carboxylase".

7. Claim 42 is objected to because of the following informalities: the term "with preceding" is grammatically incorrect and should be replaced with, for example, "with a preceding". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 39-45, 48, 50, and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claims 39 (claims 41, 42 dependent thereon) and 40 are confusing in the recitation of the term "a substantially identically-effective DNA sequence". The term is defined in the specification (see page 8, lines 10-14) as "encompassing especially functional derivations which are corresponding nucleotide sequences formed by deletions, insertions, and/or substitutions of

nucleotides whereby the enzyme activity or function remains or can even be increased". However, the scope of this "definition" is vague and it is unclear from the definition of this term what "especially functional derivations" of SEQ ID NO:1 are encompassed by the claim. The examiner has interpreted the term "a substantially identically-effective DNA sequence" to mean a polynucleotide encoding a polypeptide that has an identical enzymatic activity as the polypeptide of SEQ ID NO:2. It is suggested that Applicants clarify the meaning of the term.

10. Claims 42 and 43 recite the limitations "the regulatory sequence" in claim 42 and "these regulatory gene sequences" in claim 43. There is insufficient antecedent basis for this limitation in the claim.

11. Claims 43-45 are confusing in the recitation of the terms "one of claims 38" and "one of claim 38". The examiner has interpreted the terms as "claim 38". It is suggested that applicants clarify the meaning of the terms.

12. Claims 44 and 48 are unclear in the recitation of the terms "A gene structure containing" in claim 44 and "variety" in claim 48. It is suggested that applicants replace the terms with, for example, "A nucleic acid comprising" or "A nucleic acid consisting of" in claim 44 and "genus" in claim 48.

13. The terms "increased proportion of the central metabolism metabolites" in claim 50 and "reduced proportion of the central metabolism metabolites" in claim 51 are unclear absent a statement defining to what the levels of central metabolism metabolites are being compared. The terms "increased proportion" and "reduced proportion" are relative terms and the claims should define and clearly state as to what the levels of central metabolism metabolites are being

compared (i.e., increased or reduced in comparison to what level of central metabolism metabolites?).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 38-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 38 (claims 39-48 dependent therefrom) and 49-51 are directed to a genus of nucleic acid molecules encoding SEQ ID NO:2 or allelic variations thereof, transformed cells with deregulated enzymes that participate in the synthesis and/or export of the corresponding amino acid, and transformed cells containing an increased or reduced proportion of central metabolism metabolites. The specification defines an "allele variation" (see page 8, lines 10-14) as "encompassing especially functional derivations which are corresponding nucleotide sequences formed by deletions, insertions, and/or substitutions of nucleotides whereby the enzyme activity or function remains or can even be increased". This definition does not provide any specific information about the structure of naturally occurring (alleles) variants of SEQ ID NO:2 (e.g., regions within the polypeptide in which mutations are likely to occur). There is no description of the mutational sites that exist in nature, and there is no description of how the structure of SEQ ID NO:2 relates to the structure of any naturally occurring alleles. The general knowledge in the art concerning alleles dose not provide any indication of how one allele is

representative of unknown alleles. The nature of alleles is such that they are variant structures, and in the present state of the art, the structure of one allele does not provide guidance to the structure of others. The specification discloses only a single species of the claimed genus (i.e., the sequence encoding the polypeptide of SEQ ID NO:2) which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Furthermore, the specification teaches only two representative species of such transformed cells, i.e., *C. glutamicum* cell strains DG 52-5 and DM 368-3. Moreover, the specification fails to describe any other representative species of such transformed cells by any identifying characteristics or properties other than the functionality of being transformed cells with deregulated enzymes that participate in the synthesis and/or export of the corresponding amino acid, and transformed cells containing an increased or reduced proportion of central metabolism metabolites. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

15. Claims 38-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleic acid of SEQ ID NO:1, a nucleic acid encoding the polypeptide of SEQ ID NO:2, and microorganisms transformed with said nucleic acids, does not reasonably provide enablement for **any** "substantially identically-effective" DNA sequences of

SEQ ID NO:1, **any** allelic variations of a nucleic acid encoding the polypeptide of SEQ ID NO:2, and optionally wherein the nucleic acid has a preceding promoter of **any** "substantially-identically-effective DNA sequence" of nucleotides 20 to 109 of SEQ ID NO:1, **any** deregulated enzymes that participate in the synthesis and/or export of the corresponding amino acid, host cells containing an increased or reduced proportion of **any** central metabolism metabolites. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 38 (claims 43-48 dependent thereon), 39 (claims 41 and 42 dependent thereon), 40, and 49-51 are so broad as to encompass **any** "substantially identically-effective" DNA sequences of SEQ ID NO:1, **any** allelic variations of a nucleic acid encoding the polypeptide of SEQ ID NO:2, and optionally wherein the nucleic acid has a preceding promoter of **any** "substantially-identically-effective DNA sequence" of nucleotides 20 to 109 of SEQ ID NO:1, host cells with **any** deregulated enzymes that participate in the synthesis and/or export of the corresponding amino acid, host cells containing an increased or reduced proportion of **any** central metabolism metabolites. The scope of the claims is not commensurate with the

enablement provided by the disclosure with regard to the extremely large number of "substantially identically-effective" DNA sequences of SEQ ID NO:1, allelic variants of a nucleic acid encoding the polypeptide of SEQ ID NO:2, host cells with deregulated enzymes that participate in the synthesis and/or export of the corresponding amino acid, and host cells containing an increased or reduced proportion of central metabolism metabolites broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleic acid of SEQ ID NO:1, a nucleic acid encoding the polypeptide of SEQ ID NO:2, and microorganisms transformed with said nucleic acids.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within an encoded protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass **any** "substantially identically-effective" DNA sequences of SEQ ID NO:1, **any** allelic variations of a

nucleic acid encoding the polypeptide of SEQ ID NO:2, and optionally wherein the nucleic acid has a preceding promoter of **any** "substantially-identically-effective DNA sequence" of nucleotides 20 to 109 of SEQ ID NO:1, host cells with **any** deregulated enzymes that participate in the synthesis and/or export of the corresponding amino acid, host cells containing an increased or reduced proportion of **any** central metabolism metabolites because the specification does not establish: (A) regions of the nucleic acid of SEQ ID NO:1, a nucleic acid encoding the polypeptide of SEQ ID NO:2, or the promoter of nucleotides 20 to 109 of SEQ ID NO:1 that may be modified without affecting activity; (B) the general tolerance of pyruvate carboxylase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues of an encoded pyruvate carboxylase with an expectation of obtaining the desired biological function; (D) a rational and predictable scheme for making and using any host cells with **any** deregulated enzymes that participate in the synthesis and/or export of the corresponding amino acid and host cells containing an increased or reduced proportion of **any** central metabolism metabolites; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of **any** "substantially identically-effective" DNA sequences of SEQ ID NO:1, **any** allelic variations of a nucleic acid encoding the polypeptide of SEQ ID NO:2, and optionally wherein the nucleic acid has a preceding promoter of **any** "substantially-identically-effective DNA sequence" of nucleotides 20 to 109 of SEQ ID NO:1, host cells with **any** deregulated enzymes that participate in the synthesis

and/or export of the corresponding amino acid, host cells containing an increased or reduced proportion of **any** central metabolism metabolites. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 38-40 and 44-48 are rejected under 35 U.S.C. 102(a) as being anticipated by Peters-Wendisch et al. (IDS Reference AT; Microbiol 144:915-927). Claims 38-40 and 44-48 are drawn to a nucleic acid encoding the polypeptide of SEQ ID NO: 2 and/or allelic variants thereof, and optionally, wherein the nucleic acid has an upstream promoter of nucleotides 20 to 109 of SEQ ID NO: 1 or a substantially identically-effective DNA sequence thereof; the nucleic acid of nucleotides 165 to 3587 of SEQ ID NO: 1 or a substantially identically-effective DNA sequence thereof; a gene structure, vector, and host cells containing a nucleic acid encoding the polypeptide of SEQ ID NO: 2 and/or allelic variants thereof, and optionally wherein the host

cells are of the genus *Corynebacterium*; and host cells containing a vector containing a nucleic acid encoding the polypeptide of SEQ ID NO: 2 and/or allelic variants thereof.

Peters-Wendisch et al. teach a pyc gene that is 100 % identical to nucleotides 1 to 3728 of SEQ ID NO:1 that encodes a polypeptide that is 100 % identical to SEQ ID NO:2 (see page 919, sequence comparison). Peters-Wendisch et al. further teach insertion of the pyc gene into vectors for cloning, expression, and homologous recombination (page 916, Table 1) and transformation of *C. glutamicum* with said vectors. This anticipates claims 38-40 and 44-48 as written.

Should Applicants present an argument that the reference of Peters-Wendisch et al. cannot be applied in a rejection under 35 U.S.C. 102(a) due to the date of the publication, Applicants should provide an English translation of the priority documents submitted with the instant application (German Application No. 19743894.6 and German Application No. 19831609.7).

17. Claims 38-40 and 44-47 are rejected under 35 U.S.C. 102(a) as being anticipated by Koffas et al. (Appl Microbiol Biotechnol 50:346-352; published on the internet on 24 September 1998). Claims 38-40 and 44-48 are drawn to a nucleic acid encoding the polypeptide of SEQ ID NO:2 and/or allelic variants thereof, and optionally, wherein the nucleic acid has an upstream promoter of nucleotides 20 to 109 of SEQ ID NO: 1 or a substantially identically-effective DNA sequence thereof; the nucleic acid of nucleotides 165 to 3587 of SEQ ID NO: 1 or a substantially identically-effective DNA sequence thereof; a gene structure, vector, and host cells containing a nucleic acid encoding the polypeptide of SEQ ID NO:2 and/or allelic variants thereof, and

optionally wherein the host cells contain a vector containing a nucleic acid encoding the polypeptide of SEQ ID NO: 2 and/or allelic variants thereof.

Koffas et al. teach a pyc gene that is 100 % identical to nucleotides 10 to 3603 of SEQ ID NO:1 that encodes a polypeptide that is 99.9 % identical to amino acids 2 to 1140 of SEQ ID NO:2 (see page 350, Figure 3). Koffas et al. further teach insertion of the pyc gene into vectors for cloning (page 347) and transformation of *E. coli* (page 347). This anticipates claims 38-40 and 44-47 as written.

Should Applicants present an argument that the reference of Koffas et al. cannot be applied in a rejection under 35 U.S.C. 102(a) due to the date of the publication, Applicants should provide an English translation of the priority documents submitted with the instant application (German Application No. 19743894.6 and German Application No. 19831609.7).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claims 41-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peters-Wendisch et al. or Koffas et al. in view of de Boer et al. (Proc Natl Acad Sci U S A 80:21-5). Claims 41-43 are drawn to a nucleic acid encoding SEQ ID NO:2 and/or allelic variants thereof or the nucleic acid of nucleotides 165 to 3587 of SEQ ID NO: 1 or a substantially identically-

effective DNA sequence thereof with an upstream tac promoter, and optionally with the regulatory sequences associated with the tac promoter.

Peters-Wendisch et al. and Koffas et al. disclose the teachings as described above.

de Boer et al. teach two tac promoters, tacI and tacII (page 23), derived from the trp and lac UV5 promoters that are useful for bacterial expression of polypeptides. de Boer et al. further teach the tacI and tacII promoters increased transcription 11 and 7 fold, respectively, relative to the lac UV5 promoter and 3 and 2 fold, respectively, relative to the trp promoter (page 21, abstract). Both the tac promoters have a –35 sequence and a Pribnow box as promoter regulatory sequences.

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Peters-Wendisch et al. or Koffas et al. and de Boer et al. for a nucleic acid encoding SEQ ID NO:2 and/or allelic variants thereof with an upstream tac promoter or the nucleic acid of SEQ ID NO:1 or a substantially identically-effective DNA sequence thereof with an upstream tac promoter, and optionally with the regulatory sequences associated with the tac promoter. One would have been motivated for said nucleic acids with a tac promoter, and optionally, the regulatory sequences associated therewith because of the increased expression from a tac promoter relative to either trp or lac UV5 promoters as described above. One would have a reasonable expectation of success for a nucleic acid encoding SEQ ID NO:2 and/or allelic variants thereof or the nucleic acid of nucleotides 165 to 3587 of SEQ ID NO: 1 or a substantially identically-effective DNA sequence thereof with an upstream tac promoter, and optionally with the regulatory sequences associated with the tac promoter because of the results

of Peters-Wendisch et al. or Koffas et al. and de Boer et al. Therefore, claims 41-43, would have been obvious to one of ordinary skill in the art.

19. Claims 49-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koffas et al. in view of Eikmanns et al. (Antonie Van Leeuwenhoek 64:145-63). Claims 49-51 are drawn to the host cells as encompassed by the claims transformed with a nucleic acid encoding SEQ ID NO:2 and/or allelic variants thereof in replicable form.

Koffas et al. disclose the teachings as described above. Koffas et al. further teach that pyc is an important anaplerotic enzyme for replenishing oxaloacetate consumed during lysine and glutamic acid production in industrial fermentations (page 346, abstract).

Eikmanns et al. teach that deregulation of the lysC gene encoding aspartate kinase in the C. glutamicum strain MH20-22B led to significantly increased yields of lysine (a C. glutamicum strain with high lysine productivity produced by mutagenesis with feedback resistant aspartate kinase and phosphoenolpyruvate carboxylase enzymes and significantly lower citrate synthase and pyruvate kinase activities, thereby increasing or decreasing levels of metabolites involved in amino acid biosynthesis, accordingly (page 153, left column).

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Koffas et al. and Eikmanns et al. for a host cell as taught by Eikmanns et al. transformed with the nucleic acid of Koffas et al. in a replicable vector. One would have been motivated for the host cell of Eikmanns et al. transformed with the nucleic acid of Koffas et al. in a replicable vector in order to obtain a host cell with increased lysine production. One would have a reasonable expectation of success for the host cell of Eikmanns et al. transformed with the

nucleic acid of Koffas et al. in a replicable vector because of the results of Koffas et al. and Eikmanns et al. Therefore, claims 49-51, drawn to the host cells as set forth in the claims transformed with a nucleic acid encoding SEQ ID NO:2 and/or allelic variants thereof in replicable form would have been obvious to one of ordinary skill in the art.

Conclusion

20. No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:30 am to 2:00 pm and from 3:30 pm to 5:30 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600